

· 综述 ·

童年期虐待和忽视与心身疾病的关联

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【摘要】童年期虐待和忽视可能是青少年或成年期罹患心身疾病的危险因素, 推测可能与心理创伤所致的免疫功能失调、非稳态负荷、大脑结构和功能改变等因素有关。现就童年期虐待和忽视与心身疾病的关联进行综述。

【关键词】童年期; 虐待; 忽视; 心身疾病; 相关机制; 关联; 综述

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【Abstract】Childhood abuse and neglect may be the risk factors for psychosomatic diseases in adolescence or adulthood, which may be related to immune dysfunction, allostatic load, brain structure and function changes. This article reviews the relationship between childhood abuse and neglect and psychosomatic diseases.

【Key words】Childhood; Abuse; Neglect; Psychosomatic diseases; Relevant mechanism; Association; Review

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心身疾病(psychosomatic diseases)又称心理生理疾病,是一组与心理社会因素密切相关的疾病,如原发性高血压、糖尿病、消化性溃疡、支气管哮喘及癌症等。有关发达国家的调查发现,在综合医院的初诊患者中,约 1/3 的就诊患者为心身疾病^[1]。心身疾病由多种因素所致,童年期虐待和忽视作为心身疾病的心理社会因素逐渐得到人们的关注。童年期是人类生理心理发展的黄金时段,此期暴露不良经历可能对儿童青少年或成年后的身心健康有着潜在的影响。众所周知,童年期虐待与个体罹患精神障碍有关^[2-3]。一些研究发现,童年期虐待和忽

视也可能是青少年或成年期罹患心身疾病的危险因素,会显著增加心身疾病的患病风险。童年期虐待和忽视是指早期生命中的负面经历,包括躯体虐待、情感虐待、性虐待、躯体忽视和情感忽视^[4]。WHO 的调查表明,1/3 以上的人经历过童年期虐待和忽视^[5],其影响可能会贯穿于全生命周期。本文就童年期虐待和忽视与心身疾病的关联及其机制进行综述,旨在为心身疾病的干预和管理提供理论依据。

一、童年期虐待和忽视与心身疾病

1. 童年期虐待和忽视与心血管疾病:近年来,我国在治疗和预防心血管疾病方面取得了较大进

展,但心血管疾病仍然具有高患病率和病死率^[6]。目前的研究表明,童年期虐待和忽视与心血管疾病有关。一项系统综述显示,在心血管疾病终点的 24 项研究中,90% 以上的患者的心血管疾病与其所经历的童年期虐待和忽视关联,同时发现 61.5% 的患者的不良童年经历与高血压有关^[7]。童年期虐待和忽视会导致机体血压调节障碍,出现夜间血压升高或昼高夜低的血压节律紊乱^[8]。Su 等^[9]的纵向研究调查了虐待和忽视对童年期到青年期的血压轨迹的影响,结果发现暴露于多次虐待和忽视的人的血压上升速度明显高于无童年期虐待和忽视者。但 Gooding 等^[10]的研究中并未发现童年期虐待和忽视与成年早期血压升高有关,其认为影响血压不是单一的因素,如压力性肥胖或不良的生活方式也会导致成年早期高血压,而童年期的创伤暴露可能存在潜在的持续影响。此外,研究者发现童年期虐待和忽视对心血管疾病的影响存在性别差异,童年期不良经历与女性和早年发生心血管疾病(< 50 岁)之间存在更强的关联性^[11]。童年期虐待和忽视的事件类型对血管性疾病通常有不同的影响,童年期经历情感虐待发生偏头痛的可能性更大^[12-13],而性虐待与成年期心肌梗死呈正相关;躯体虐待与男性心肌梗死的相关性更大,而在女性中未观察到这种关联^[14]。研究还发现心血管疾病的发生与创伤事件之间存在剂量-反应关系,每增加一种创伤事件,心血管疾病的发生率可增加 7.8%^[15]。进一步研究发现,焦虑/抑郁、吸烟、体重指数(body mass index, BMI)和炎症因子介导了不良童年经历和心血管疾病之间的中介效应(26%~90%)^[16]。综上所述,童年期虐待和忽视是心血管系统疾病发生的重要危险因素,且童年期虐待和忽视的事件类型和数量与心血管疾病存在剂量-反应关系。

2. 童年期虐待和忽视与内分泌疾病:研究发现,童年期虐待和忽视与成年期持续代谢失调相关^[17-18]。糖尿病是一种慢性代谢性疾病,全球患病率为 9.3%^[19]。一项前瞻性队列研究发现,童年期虐待和忽视可增加成年后患糖尿病的风险,每增加一次创伤事件,患糖尿病的可能性增加 11%^[20]。目前的研究表明,虐待和忽视的不同类型与糖尿病的关联差异很大,躯体虐待和性虐待是个体成年后罹患糖尿病的重要危险因素^[21]。不良的童年经历不但增加糖尿病的患病风险,还会增加糖尿病共病抑郁症的可能性^[22]。童年期虐待和忽视与个体成年后的超重和肥胖也密切相关,肥胖者经历创伤事件的概率为

68.8%,而非肥胖者为 38.8%^[23]。值得注意的是,具有童年期虐待和忽视的人在生命早期就出现了体重问题^[24]。Wiss 等^[25]的研究结果强调,暴露于多种创伤事件后,肥胖的概率增加 46%。童年期虐待和忽视与肥胖的严重程度也有一定关系,线性回归结果显示,BMI 增加者的童年期创伤量表评分较高^[26]。研究者认为,BMI 增加与创伤之间的关系可归因于食物成瘾,这很可能是个体对创伤的一种进食应对反应,也可能与进食的脑区功能联结异常相关^[27]。上述研究结果强调,应当提高对童年期虐待和忽视影响的评估,建立规律性锻炼和健康的生活方式,以降低内分泌疾病的发生率。

3. 童年期虐待和忽视与炎症性疾病:童年期虐待和忽视会促进慢性炎症性疾病的发生和发展,Wan 等^[28]的研究发现,童年期遭受虐待会增加罹患免疫介导的炎症性疾病(immune-mediated inflammatory disorders, IMID)的风险,如多发性硬化症、炎症性肠病和类风湿性关节炎等,其中情感虐待与 IMID 之间有明显的相关性。此外,患有风湿性疾病(强直性脊柱炎、类风湿性关节炎和结缔组织病)的患者的儿童期创伤问卷得分明显高于健康对照组^[29],表明创伤事件在风湿性疾病的发病中起着一定作用。纤维肌痛是一种病因不明,以广泛的肌肉骨骼疼痛为特征的慢性疾病。荟萃分析证实,童年期虐待和忽视与成人纤维肌痛有关,其中以躯体虐待相关性最强^[30]。虐待和忽视的严重程度也影响着炎症性疾病的治疗反应和预后,诊疗时可将心理社会干预作为炎症性疾病治疗的一个组成部分。

4. 童年期虐待和忽视与癌症:癌症是目前全球死亡的第二大原因,研究人员发现童年期虐待和忽视对癌症有一定的影响。Hovdestad 等^[31]的研究显示,童年期虐待和忽视与女性癌症之间存在显著正相关,而男性则不存在。多种类型的创伤事件会增加女性的患癌风险,其中躯体虐待的严重程度和频率与癌症之间存在明显的剂量-反应关系。另一项研究表明,在多种创伤类型中,躯体虐待和性虐待与成年期癌症发生呈正相关,当暴露 2 种以上童年期虐待或忽视事件类型时,成年人癌症发生的风险显著增加^[32]。Bower 等^[33]提出,童年期虐待和忽视与早期乳腺癌患者的炎症信号表达升高以及广泛的免疫失调有关,具体表现在经典核因子 κ B(nuclear factor kappa-B, NF- κ B) 相关促炎症信号通路以及 I 型干扰素系统的增强有关。上述研究结果表明,积极预防童年期创伤事件的发生,并对有创伤经历

的人群加强干预是有必要的,这对解决与癌症相关的健康问题具有临床意义。

二、童年期虐待和忽视与心身疾病的神经生物学机制

虽然大多数研究表明,童年期虐待和忽视与心身疾病相关,但作用机制并不十分明确,可能的机制如下。

1. 免疫功能失调: 童年期虐待和忽视会促使机体产生过度的免疫反应,而炎性介质又会进一步导致机体免疫抑制、氧化应激和细胞毒性反应,这些与心身疾病的发生有关。童年期虐待和忽视与炎性标志物升高显著相关,特别是与TNF- α 和CRP关系密切。不同类型的创伤事件影响着机体炎症反应特征,如躯体虐待和性虐待与TNF- α 和IL-6的升高有关^[34];也有研究提示情感虐待与IL-6水平升高相关^[35]。CRP、纤维蛋白原和白细胞计数升高是心血管疾病常见的炎性标志物,一项纵向前瞻性研究表明,童年期虐待和忽视与3者的升高有关,可能触发了心血管疾病的发生^[36]。总之,童年期虐待和忽视会导致机体的高炎症表达,引起的免疫系统失调可能是发生心身疾病的一种催化剂,增加了心身疾病的患病风险。

2. 神经内分泌紊乱: 反复或长期暴露于童年期虐待和忽视,管理压力和情绪调节的脑区可能产生应激反应系统的超敏性,导致应激反应功能亢进,最终可能发生心身疾病^[37-39]。下丘脑-垂体-肾上腺(hypothalamic-pituitary-adrenal, HPA)轴是机体调控应激反应的主要机制,创伤事件会引发HPA轴的过度反应,促使炎性标志物及血液中甘油三酯、游离脂肪酸和葡萄糖水平的升高,所有这些都与糖尿病、高脂血症等慢性病的发生、发展有关^[40]。童年期虐待和忽视会影响HPA轴负反馈失调以及皮质醇过度反应^[41],皮质醇水平升高对免疫系统和代谢都有直接或间接的影响,如高皮质醇水平会增加胰腺细胞的抵抗^[42],促发糖尿病的发生。此外,童年期虐待和忽视还会导致肾素-血管紧张素-醛固酮系统(renin-angiotensin-aldosterone-system, RAAS)严重失调,并且对RAAS系统有持续性累积效应,醛固酮和肾素水平的长期升高会增加高血压和心血管疾病的发生风险^[43-44]。Danese等^[45]的研究发现,童年期虐待和忽视会导致交感神经和副交感神经的功能紊乱,造成自主神经系统调节功能失衡。长期过度激活神经内分泌轴会导致人体免疫、内分泌等系统紊乱,使人体处于超负荷的应激状态,不利于个体的身心健康。

3. 非稳态负荷(allostatic load): 内环境稳态是机体适应环境压力时的一种动态调节状态。当内环境超越自我的适应能力时则会造成机体各系统的失调,从而导致器官的病理性变化和慢性疾病^[46]。非稳态负荷模型提示,在慢性应激的环境下,调节系统(神经、内分泌、免疫系统等)的累积性损害会增加罹患心身疾病的风险。童年期虐待和忽视的神经生物学模型显示,长期暴露于压力或创伤事件中会导致稳态系统的生物性“磨损”^[47],如反复暴露创伤性事件会使糖皮质激素受体产生持续性适应反应,造成糖皮质激素代谢紊乱和胰岛素的抵抗^[48],最终发展为心脏代谢性疾病。在中年女性中,童年期躯体虐待和性虐待与多种氨基酸和脂质水平异常有明显的相关性,其中谷氨酸和酪氨酸循环水平的升高与糖尿病和心血管疾病风险的增加密切相关^[17]。长期的应激状态会导致高水平的非稳态负荷,这是心身疾病发生的重要危险因素。

4. 脑结构和功能改变: 童年期虐待和忽视加剧了躯体重要脏器直接或间接的压力反应^[49]。童年期的创伤经历可能会引起大脑结构或功能的改变。研究发现,童年期创伤会导致杏仁核体积减小,并且性虐待与杏仁核高反应性有关^[50],而情感虐待更有可能造成前额叶-边缘系统异常^[51]。Paquola等^[52]的研究发现,与非创伤组相比,创伤组海马体积明显减小,其中躯体虐待和性虐待对海马体体积的影响更显著,此外,该研究还发现有童年期创伤史的成年人表现出3组灰质体积的减小,分别为右侧背外侧前额叶皮质、右海马和右中央后回,这些结构的改变对患者的记忆、认知、信息处理等功能有不利影响,与有童年期创伤经历的人更容易出现阴性认知相关。白质束在连接在大脑区域之间的信息传递中起关键作用,调节整个神经网络的激活速度和时间。研究发现,童年期虐待和忽视与白质微结构异常相关,尤其是穹窿、胼胝体和视辐射,上述结构完整性的减弱可能会妨碍情绪和视觉感官功能,损害恐惧消退记忆,从而使个体容易受到心理病理学的影响^[53]。Zhong等^[54]的研究结果表明,童年期虐待和忽视除了会引起大脑结构的改变,还会使大脑功能对创伤反应产生远期影响,在神经功能方面出现背外侧前额叶和岛叶的激活显著增加,使个体表现出更强的主观痛苦和皮质醇水平的升高。儿童和青少年是神经发育的关键时期,早期不良经历对控制代谢稳态和行为的脑功能和神经生物学结构有相当大的不利影响。童年期虐待和忽视与心身疾病的

可能机制,除了免疫功能失调、脑结构和功能的改变、神经内分泌紊乱和非稳态负荷之外,还与不良的认知模式和生活方式等有关,不良的认知心理模式包括认知脆弱性的增加、压力感知的增强、社会支持感知的减少和情绪幸福感的降低等^[55],上述不良的心理行为也可能在早年创伤与心身疾病之间起着诱导作用。除此之外,吸烟、物质滥用、缺乏体育锻炼、不健康的饮食等危险健康行为与不良童年经历的数量呈正相关^[56],而这些不良的生活方式与心身疾病的发生密切相关。

三、早期预防和治疗

鉴于童年期虐待和忽视对心身健康的远期影响,在诊疗中应详细评估童年期的创伤事件,建立循证育儿和青少年健康成长指导计划,改善家庭教养模式和学校管理方式,提高青少年的积极认知水平和心理弹性,并加强宣教,进行早期预警、管理和应激的干预。

早期预防不良童年经历将大大减少人群中许多危害健康行为的发生,在治疗慢性病群体时应高度关注对童年期虐待和忽视事件的评估,提供心理咨询服务和心理健康教育,提高心身疾病患者的认知模式和心理调节能力^[57]。对于已经接受针对心血管疾病药物治疗的患者,减少童年期虐待和忽视的负担可能有助于进一步减轻残余的心血管疾病症状^[58]。对于伴有童年期创伤的患者,在药物治疗的同时,联合认知治疗改变患者的负性认知模式,可能更有利于患者心身健康的痊愈。社会支持和正念疗法已被证实是一种保护性因素,用于减轻或缓解创伤事件造成的心身损害^[59-60]。在临床就诊期间明确童年期虐待和忽视暴露情况后可在适当的时机转诊至心理服务进行专业的诊疗。

四、总结与展望

童年期虐待和忽视与心身疾病密切相关,创伤事件可导致个体的认知改变、神经内分泌失调、非稳态负荷、神经内分泌紊乱等改变,这些可能是心身疾病发生的易感因素,需进一步深入探讨其生物-心理-社会的交互作用机制。关于童年期虐待和忽视与心身疾病之间的关系,目前的研究结果受样本量、受试者种族、病史采集等相关因素的影响,研究结论存在一定差异。此外,大多数研究都是横断面研究,可能存在信息的偏倚。未来的研究需扩大样本,设计童年期虐待和忽视与心身疾病的前瞻性研究,明确其中的主要发病机制,尽量减少混杂因素的影响。

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